

**U.S.S.N. 09/903,327**  
**NEMEROW *et al.***  
**AMENDMENT**

**CLAIMS:**

A listing of the claims, in accord with 37 CFR §1.121, is provided. The listing of claims replaces all prior such listings of claims. Claims 2-16, 18-27, 30, 32-34, 36 and 37 are amended and claims 40-45 are added herein. Claims 1, 17, 29, 31, 38 and 39 are cancelled herein without prejudice or disclaimer herein.

1. (Currently cancelled)
2. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted vector delivery particle of claim 32, wherein the targeting agent or portion thereof that triggers phosphatidylinositol-3-OH kinase (PI3K) activation is selected from the group consisting of proteins that bind to G-protein coupled receptors.
3. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 32, wherein the ~~bifunctional molecule, further comprising~~ comprises a linker that links the antibody or antigen-binding portion thereof to the targeting agent.
4. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 32, wherein the ~~bifunctional molecule that~~ comprises a fusion protein.
5. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 32, wherein the ~~bifunctional molecule that~~ comprises chemically conjugated polypeptides.
6. (Currently amended) The ~~bifunctional molecule~~ targeted delivery vector particle of claim ~~2~~ 3, wherein the linker is a single amino acid or a peptide.
7. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 32, wherein the antibody comprises a heavy chain or a portion thereof sufficient for antigen-binding fused to the targeting agent.
8. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 32, wherein the antibody portion is an Fab'2 fragment.

**U.S.S.N. 09/903,327**  
**NEMEROW *et al.***  
**AMENDMENT**

9. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 32, wherein the antibody portion comprises a sufficient portion of the variable regions of the heavy and light chains for antigen recognition.

10. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 32, wherein the antibody comprises the sequence of amino acids set forth in SEQ ID No. 2 or SEQ ID No. 6 or a sufficient portion thereof for antigen recognition.

11. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 32, wherein the antibody comprises the sequence of amino acids set forth in SEQ ID No. 4 or a sufficient portion thereof for antigen recognition.

12. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 32, wherein the antibody portion is an Fab fragment.

13. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 10, wherein ~~the nucleic acid encoding the antibody portion is encoded by a sequence of nucleic acids that include a sequence of nucleic acids~~ selected from among:

(a) the coding portion of the sequence of nucleotides set forth in SEQ ID No. 1 or SEQ ID No.5;

(b) a sequence of nucleotides that comprises one or more degenerate codons of (a); and

(c) a sequence of nucleotides that hybridizes along its full length under conditions of high stringency to a sufficient portion of (a) or (b) to encode an antigen-binding portion of the antibody.

14. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 11, wherein ~~the nucleic acid encoding the antibody~~

**U.S.S.N. 09/903,327**  
**NEMEROW *et al.***  
**AMENDMENT**

portion is encoded by a sequence of nucleic acids that include a sequence of nucleic acids selected from among:

(a) the coding portion of the sequence of nucleotides set forth in SEQ ID No. 3;

(b) a sequence of nucleotides that comprises one or more degenerate codons of (a); and

(c) a sequence of nucleotides that hybridizes along its full length under conditions of high stringency to a sufficient portion of (a) or (b) to encode an antigen-binding portion of the antibody.

15. (Currently amended) The ~~bifunctional molecule of claim 1, comprising~~ targeted delivery vector particle of claim 32, wherein the bifunctional molecule comprises the sequence of amino acids set forth in any of SEQ ID Nos. 7-14 for specific binding to a targeted receptor.

16. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 32, wherein the protein that binds to  $\alpha_v$  integrin is a viral protein ~~or a bacterial protein~~ that interacts with  $\alpha_v$  integrins for internalization of the ~~respective virus or bacteria~~.

17. (Currently cancelled)

18. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 32, wherein the antibody or portion thereof specifically binds to the penton base or penton fiber or the complex thereof of an adenovirus.

19. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 32, wherein the antibody or portion thereof specifically binds to an antigen that includes an RGD motif.

20. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 32, wherein the targeting agent comprises all or sufficient portion thereof of a protein that binds to G-protein coupled receptors,

**U.S.S.N. 09/903,327**  
**NEMEROW *et al.***  
**AMENDMENT**

oncogene product receptors, hormone receptors or cytokine receptors that employ the PI3 signaling pathway for signal transduction,

wherein the sufficient portion thereof specifically binds to the cell surface receptor therefor and internalizes linked viral ~~or bacterial~~ particles.

21. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 32, wherein the targeting agent comprises all or sufficient portion thereof of a protein that binds to G-protein coupled receptors that employ the PI3 signaling pathway for signal transduction,

wherein the sufficient portion thereof specifically binds to the cell surface receptor therefor and internalizes linked viral ~~or bacterial~~ particles.

22. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 32, wherein the targeting agent comprises all or sufficient portion thereof of hormone or growth factor or cytokine,

wherein the sufficient portion thereof ~~is specifically bind~~ binds to the cell surface receptor therefor and internalizes linked viral ~~or bacterial~~ particles.

23. (Currently amended) The ~~bifunctional molecule~~ targeted delivery vector particle of claim 6, wherein the targeting agent or portion thereof is a tumor necrosis factor (TNF), ~~an~~ a fibroblast growth factor (FGF), an insulin-like growth factor ~~(IGF)~~ (IGF), a colony stimulating factor (CSF), insulin or a ~~serum~~ stem cell factor (SCF).

24. (Currently amended) The ~~bifunctional molecule~~ targeted delivery vector particle of claim 6, wherein the targeting agent or portion thereof is insulin, insulin-like growth factor-1 (IGF-1), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), stem cell factor (SCF), colony stimulating factor (CSF), a platelet-derived growth factor (PDGF), ~~an~~ a fibroblast growth factor (FGF), a heparin binding epidermal growth factor (HBEGF), a vascular endothelial growth factor (VEGF) or dimer thereof.

25. (Currently amended) The ~~bifunctional molecule~~ targeted delivery vector particle of claim 6, wherein the targeting agent or portion thereof is tumor

U.S.S.N. 09/903,327  
NEMEROW *et al.*  
AMENDMENT

necrosis factor- $\alpha$  (TNF- $\alpha$ ), insulin-like growth factor-1 (IGF-1), stem cell factor (SCF) or an epidermal growth factor (EGF).

26. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 32, wherein the targeted cell surface protein is selected from among a PDGF receptor, an IGF-1 receptor, an EGF receptor, a member of the FGF receptor family, a TNF receptor, a CSF-1 receptor, an insulin receptor, an IGF-1 receptor, an NGF receptor, an ~~IL-2~~ IL-2 receptor, an ~~IL-3~~ IL-3 receptor, an ~~IL-4~~ IL-4 receptor, an IgM receptor, a CD4 receptor, a CD2 receptor, a CD3/T cell receptor, a G protein linked thrombin receptor, an ATP receptor, and an fMLP receptor.

27. (Currently amended) The ~~bifunctional molecule of claim 1~~ targeted delivery vector particle of claim 32, wherein the targeted cell surface protein is selected from among tyrosine kinase receptors that, when activated, result in increased accumulation of PtdIns(3,4,5)P3, and receptors associated with the src family non-receptor tyrosine kinases that stimulate PI3Ks ~~phosphorylate phosphatidylinositol(3,4,5)P3 (PtdIns(3,4,5)P3)~~ to lead to PtdIns(3,4,5)P3 accumulation.

28. (cancelled)

29. (Currently cancelled)

30. (Currently amended) The targeted delivery vector particle of claim ~~29~~ 32, wherein the vector genome ~~gene delivery vector~~ encodes a therapeutic product.

31. (Currently cancelled)

32. (Currently amended) The A targeted delivery vector ~~of claim 29,~~ wherein the vector is particle, comprising:

(a) a fiberless adenovirus particle;

(b) a bifunctional molecule, comprising an antibody or antigen-binding portion thereof and a targeting agent, wherein:

the antibody or antigen-binding portion specifically binds to an antigen in a protein on the particle;  
the protein on the particle binds to  $\alpha_v$  integrin; and  
the targeting agent specifically binds to a cell surface protein that activates the phosphatidylinositol 3 (PI3) signaling pathway; and

(c) a fiberless adenovirus vector genome.

33. (Currently amended) The targeted delivery vector particle of claim ~~29~~ 32, wherein the bifunctional molecule and viral ~~or bacterial~~ vector particle are complexed by interaction of the antibody or antigen-binding portion of the bifunctional molecule with ~~a~~ the viral or bacterial particle surface protein.

34. (Currently amended) The targeted delivery vector particle of claim ~~29~~ 32, wherein ~~the bifunctional molecule and viral or bacterial vector wherein the~~ antibody portion of the bifunctional molecule is covalently linked to ~~the~~ a viral or bacterial particle surface protein.

35. (cancelled)

36. (Currently amended) A combination, comprising:  
a fiberless adenoviral particle ~~a delivery vector~~ for delivering gene products to targeted cells; and  
a bifunctional molecule that comprises: of claim 1  
an antibody or antigen-binding portion and a targeting agent, wherein:  
the antibody or antigen-binding portion specifically binds to an antigen in a protein on a viral particle that binds to  $\alpha_v$  integrin; and  
the targeting agent specifically binds to a cell surface protein that activates the phosphatidylinositol 3 (PI3) signaling pathway.

37. (Currently amended) The combination of claim 36, wherein:  
the bifunctional molecule and delivery vector particle for delivering gene products to targeted cells are complexed via penton in the vector particle.

38. (Currently cancelled)

**U.S.S.N. 09/903,327**  
**NEMEROW *et al.***  
**AMENDMENT**

39. (Currently cancelled)

40. (New) A fiberless adenoviral particle, comprising a bifunctional molecule of claim 10.

41. (New) A targeted delivery vector particle, comprising:

(a) a fiberless adenovirus particle; and

(b) a bifunctional molecule complexed with the particle, comprising an antibody or antigen-binding portion and a targeting agent, wherein:  
the antibody or antigen-binding portion specifically binds to an antigen in a protein on the particle;  
the protein on the particle binds to  $\alpha_v$  integrin; and  
the targeting agent specifically binds to a cell surface protein that activates the phosphatidylinositol 3 (PI3) signaling pathway.

42. (New) A bifunctional molecule, comprising:

an antibody or antigen-binding portion and a targeting agent, wherein:  
the antibody or antigen-binding portion comprises all or a portion of DAV-1 antibody, wherein the portion thereof binds to a component of penton; and  
the targeting agent specifically binds to a cell surface protein that activates the phosphatidylinositol 3 (PI3) signaling pathway.

43. (New) A fiberless adenoviral particle, comprising a bifunctional molecule of claim 42.

44. (New) The combination of claim 36 that is packaged as a kit, optionally containing instructions for use thereof.

45. (New) The targeted delivery vector particle of claim 10, wherein the antibody portion is an Fab fragment.